

REMARKS

The specification has been amended to include sequence identifiers as set forth in 37 C.F.R. § 1.821 - 1.825 where appropriate. No new matter has been added.

I. Status of the claims

Claims 1-12 are pending in the application. Claims 1-4 have been amended to insert sequence identification numbers as set forth in 37 C.F.R. § 1.821 - 1.825 where appropriate and to correct a spelling error. No new matter has been added.

II. Restriction Requirement

Applicants hereby elect to prosecute the protein DSGCKLLEDV VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN QSHRTLKNFG LMMHTVYDSI WCNL (SEQ ID NO: 3) for claims 1-9 with traverse. With regard to the traversal of the restriction requirement, Applicants respectfully assert that the Office Action has not met the burden of establishing that the groups of the restriction are patentably distinct. Furthermore, the Office Action has not established that an undue burden would be placed on the Examiner if required to search the proteins for all the claims together as opposed to separately.

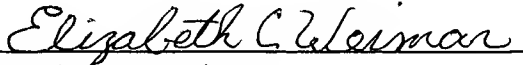
III. Conclusion:

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Except for issues payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **constructive petition for extension of time** in accordance with 37 C.F.R. § 1.136(a)(3).

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Morgan, Lewis & Bockius LLP
Customer No. **09629**
1800 M Street, N.W.
Washington, D.C. 20036
202-467-7000

Respectfully submitted
Morgan, Lewis & Bockius LLP


Elizabeth C. Weimar
Registration No. 44,478

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at page 2, line 10 has been amended as follows:

In a preferred embodiment, the disease marker is a protein, preferably a protein having a N-terminal sequence selected from:

EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG (**SEQ ID NO: 1**);

WDPKE: (**SEQ ID NO: 2**); and

DSGCKLLEDM VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN
QSHRTLKNFG LMMHTVYDSI WCNL (**SEQ ID NO: 3**).

Paragraph beginning at page 3, line 14 has been amended as follows:

In a second aspect, the present invention consists of a protein marker detectable in tears having an N-terminus selected from:

EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG (**SEQ ID NO: 1**);

WDPKE: (**SEQ ID NO: 2**); and

DSGCKLLEDM VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN
QSHRTLKNFG LMMHTVYDSI WCNL (**SEQ ID NO: 3**).

Paragraph beginning at page 3, line 20 has been amended as follows:

Preferably, the protein marker detectable in tears includes the amino acid sequence:

EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG (**SEQ ID NO: 1**);

WDPKE: (**SEQ ID NO: 2**); and

DSGCKLLEDM VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN
QSHRTLKNFG LMMHTVYDSI WCNL (**SEQ ID NO: 3**) or part thereof.

Paragraph beginning at page 6, line 27 has been amended as follows:

--The second new protein was represented by at least 5 new isoforms of different pI. Two of these were N-terminally sequenced and gave the sequence commencing EDASS (EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG (**SEQ ID NO: 1**)) (spots 1 & 2).--

Table 2 beginning on Page 7 has been amended as follows:

Spot No.	pI	Mw(k)	Sequence Tag	Identification
1	5.0	25	EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG <u>(SEQ ID NO: 1)</u>	unknown
2	4.4	25	EDASS <u>(SEQ ID NO: 4)</u>	As for No. 1
3	4.6	14	SSSKE <u>(SEQ ID NO: 5)</u>	Human Cystatin S
4	4.8	14	SSSKE <u>(SEQ ID NO: 5)</u>	As for No. 3
5	5.2	40	N-terminally blocked*	Human Zn-alpha-2-glycoprotein
9	5.1	10	¹ DSGCKLLED ¹ MVEK <u>(SEQ ID NO: 6)</u>	Similarity with Human Mammaglobin & Rat Steroid-binding proteins
10	8.0	14	WDPKE <u>(SEQ ID NO: 2)</u>	Unknown
11	5.1	18	HHLLASDEE <u>(SEQ ID NO: 7)</u>	Human Von Ebner's Gland Protein
12	5.3	18	[^] SDEE <u>(SEQ. ID NO: 8)</u>	Von Ebner's Gland Protein
14	8.5	80	GRRR <u>(SEQ ID NO: 9)</u>	Human lactotransferrin

Paragraph beginning at page 7, line 9 has been amended as follows:

¹Residues sequenced
 [10] [20] [30] [40] [50]
DSGCKLLED¹M VEKTNSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN
 [60] [70]
QSHRTLKNFG LMMHTVYDSI WCNL (SEQ ID NO: 3).

In the Claims:

Claim 1 has been amended as follows:

1. (Amended) A method of screening or detecting non-ocular disease in an animal, the method comprising obtaining a tear sample from the animal and [analysing] analyzing the tear

sample for an indicator or marker of the non-ocular disease, wherein the indicator or marker is a protein having a N-terminal amino acid sequence selected from the group consisting of:
EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG (SEQ ID NO: 1);
WDPKE (SEQ ID NO: 2); and
DSGCKLLED M VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN
QSHRTLKNFG LMMHTVYDSI WCNL (SEQ ID NO: 3).

Claim 2 has been amended as follows:

2. (Amended) The method according to claim 1 wherein the protein includes the amino acid sequence:
DSGCKLLED M VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN
QSHRTLKNFG LMMHTVYDSI WCNL (SEQ ID NO: 3), or part thereof.

Claim 3 has been amended as follows:

3. (Amended) A method of screening or detecting non-ocular disease in an animal, the method comprising the steps of:
(a) obtaining a tear sample from the animal;
(b) separating biomolecules present in the tear sample; and
(c) detecting for the presence or absence of one or more biomolecules such that the presence or absence of the one or more biomolecules being an indicator or marker of a disease state in the animal, wherein the one or more biomolecules are one or more proteins having a N-terminal amino acid sequence selected from the group consisting of:
EDASSDSTGA DPAQ(E/Q)AGTSQ PNEDIAG (SEQ ID NO: 1);
WDPKE (SEQ ID NO: 2); and
DSGCKLLED M VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN
QSHRTLKNFG LMMHTVYDSI WCNL (SEQ ID NO: 3).

Claim 4 has been amended as follows:

4. (Once Amended) The method according to claim 3 wherein the protein includes the amino acid sequence:
DSGCKLLED M VEKTINSDIS IPEYKELLQE FIDSDAAAEA MGKFKQCFLN
QSHRTLKNFG LMMHTVYDSI WCNL (SEQ ID NO: 3), or part thereof.